extracellular mammalian tumor-associated or tumor-derived RNA such as EGF RNA, EGFr RNA, her-2/neu RNA c-myc RNA or hnRNP A2/B1 RNA, or any combination thereof, in said bodily fluids.

In preferred embodiments, the methods of the invention comprise the step of amplifying and detecting extracellular EGF RNA, EGFr RNA, her-2/neu RNA, c-myc RNA, and/or hnRNP A2/B1 RNA or any combination thereof from bodily fluids of an animal, most preferably a human.

In particularly preferred embodiments, the present invention provides methods for detecting EGF RNA, or EGFr RNA, or her-2/neu RNA, or c-myc RNA, or hnRNP A2/B1 RNA, or any combination thereof in blood or a blood fraction, including plasma and serum, and other bodily fluids. In these embodiments, the method comprises the steps of extracting mammalian RNA from blood, plasma, serum, or other bodily fluid, wherein a fraction of the extracted RNA comprises extracellular EGF RNA, EGFr RNA, her-2/neu RNA, c-myc RNA, or hnRNP A2/B1 RNA; or any combination thereof; *in vitro* amplifying RNA or cDNA corresponding thereto encoding EGF, EGFr, her-2/neu , c-myc, or hnRNP A2/B1 or any combination thereof; and detecting the amplified products produced from said mRNA or cDNA.

In a first aspect of this embodiment, the present invention provides methods for detecting EGF RNA, EGFr RNA, her-2/neu RNA, c-myc RNA, hnRNP A2/B1 or any combination thereof in blood or blood fractions, including plasma and serum, in an animal, most preferably a human. Said methods advantageously permit detection, diagnosis, monitoring, treatment, or evaluation of proliferative disorders, particularly stages of neoplastic disease, including premalignancy, early cancer, non-invasive cancer, carcinoma *in-situ*, invasive cancer, metastatic cancer and advanced cancer, as well as benign neoplasms. In this aspect, the method comprises the steps of extracting

mammalian RNA from blood or blood plasma or serum, *in vitro* amplifying qualitatively or quantitatively a fraction of the extracted RNA or the corresponding cDNA wherein said fraction comprises EGF-, EGFr-, her-2/neu-, c-myc-, or hnRNP A1/A2-encoding RNA or combination thereof, and detecting the amplified products of said RNA or cDNA.

The invention in a second aspect provides methods for detecting EGF-, EGFr-, her-2/neu, -c-myc-, or hnRNP A2/B1-encoding RNA or any combination thereof in any bodily fluid. Preferably, said bodily fluid is whole blood, blood plasma, serum, urine, effusions, ascitic fluid, amniotic fluid, saliva, cerebrospinal fluid, cervical secretions, vaginal secretions, endometrial secretions, gastrointestinal secretions, bronchial secretions including sputum, secretions or washings from the breast, and other associated tissue washings from an animal, most preferably a human. In this aspect, the method comprises the steps of extracting mammalian RNA from the bodily fluid; *in vitro* amplifying in a qualitative or quantitative fashion a fraction of the extracted RNA, wherein said fraction comprises extracellular EGF RNA, EGFr RNA, her-2/neu RNA, c-myc RNA, hnRNP A2/B1 RNA or any combination thereof, or more preferably cDNA corresponding thereto, and detecting the amplified product of said RNA or cDNA.

In these embodiments, the inventive methods are particularly advantageous for detecting, diagnosing, monitoring, treating, or evaluating proliferative disorders in an animal, most preferably a human, said proliferative disorders particularly including stages of neoplastic disease, including premalignancy, early cancer, non-invasive cancer, carcinoma-in-situ, invasive cancer, metastatic cancer and advanced cancer as well as benign neoplasm.

Thus, in another aspect the invention provides methods for evaluating an animal, most preferably a human, for premalignant or malignant states, disorders, or conditions. The inventive methods comprise detecting extracellular mammalian tumor-associated or tumor-derived RNA

including EGF RNA, EGFr RNA, her-2/neu RNA c-myc RNA and hnRNP A2/B1 RNA or any combination thereof in bodily fluids, preferably blood and most preferably blood plasma and serum as well as in other bodily fluids, preferably urine, effusions, ascites, amniotic fluid, saliva, cerebrospinal fluid, cervical, vaginal, and endometrial secretions, gastrointestinal secretions, bronchial secretions, breast fluid, and associated tissue washings and lavages.

The methods of the invention are also useful for identifying EGF-, EGFr-, her-2/neu-, c-myc-, or hnRNP A2/B1-expressing cells or tissue in an animal, most preferably a human. In these embodiments, detection of an *in vitro* amplified product of EGF RNA, EGFr RNA, her-2/neu RNA, c-myc RNA, or hnRNP A2/B1 RNA or cDNA corresponding thereto using the methods of the invention indicates the existence of EGF, EGFr, her-2/neu, c-myc, or hnRNP A2/B1-expressing cells or tissue in a human.

The invention further provides diagnostic kits for detecting EGF RNA, EGFr RNA, her-2/neu RNA, c-myc RNA, hnRNPA2/B1 RNA or any combination thereof in bodily fluid, preferably blood plasma or serum, wherein the kit comprises oligonucleotide primers, probes, or both primers and probes for amplifying and detecting said EGF RNA, EGFr RNA, her-2/neu RNA, c-myc RNA, hnRNPA2/B1 RNA or any combination thereof or cDNA derived therefrom. In advantageous embodiments, the kit may further comprise instructions and reagents for performing methods for extracting RNA from the bodily fluid, reverse-transcribing said RNA into cDNA or reagents for performing *in vitro* amplification.

In preferred embodiments of the inventive methods, EGF RNA, EGFr RNA, her-2/neu RNA, c-myc RNA, hnRNP A2/B1 RNA or any combination thereof is extracted from whole blood, blood plasma or serum, or other bodily fluids using any effective extraction method including but not limited to gelatin extraction methods; silica, glass bead, or diatom extraction